REMARKS

The Claims

Claims 61-67 and 69-76 are currently pending in the application. Claims 61 and 69 have been amended to recite administration of a nucleic acid rather than administration of an expression vector comprising a nucleic acid. In addition, Claims 61 and 69 have been amended to recite a nucleic acid encoding an osteoprotegerin polypeptide of amino acid residues 1 to 401 or 22 to 401 of Figure 9C-9D (SEQ ID NO:124) or a nucleic acid encoding an osteoprotegerin polypeptide comprising a deletion of from 1 to 216 amino acids from the carboxy terminus. Claims 62 and 70 have been cancelled without prejudice or disclaimer. The claim amendments do not introduce new matter or raise new issues requiring further consideration and/or search. Upon entry of the amendments, Claims 61, 63-67, 69 and 71-76 will be pending in the application.

Rejection under 35 U.S.C. 112

Claims 61-67 and 69-76 are rejected under 35 U.S.C. 112, first paragraph, as the specification allegedly does not enable one to make and/or use the invention without undue experimentation.

The Examiner argues that "although the identification and characterization of OPG and its biological activity is 'essential' for practice (sic) of the invention, the identified OPG by itself is insufficient for practice (sic) the instantly claimed invention in view of the state of the art at the time of the effective filing date". Citing references already of record, in particular Robbins et al, Orkin et al, Bolon et al., Crystal et al., Miller et al., Deonarain et al., Baylink et al. and Anderson, the Examiner argues that the art of gene therapy was still "undeveloped" and "neither routine nor accepted". It is also asserted that the nature of the transgenes, the vector construct used, means of delivery, and models and criteria for evaluation are all contributing to the "novel aspects" of gene therapy, and were not routine as of the filing date.

As admitted by the Examiner, the present specification provides the essential teachings for carrying out the invention. These teachings include the identification of a nucleic acid encoding an OPG polypeptide, a determination of the activity of OPG in inhibiting bone resorption, and methods for determining OPG activity *in vitro* and *in vivo*. In order to carry out a gene therapy experiment, one needs only the appropriate expression vector and method of delivering the nucleic acid construct to the animal. The Sheng declaration clearly showed that using the information provided in the specification, together with the use of a publicly available vector and a delivery route that were known to one of skill in the art, one could administer to an animal a nucleic acid encoding OPG and obtain expression such that bone resorption was inhibited. Contrary to the Examiner's position, there is nothing in the Sheng declaration that "supplements" the original disclosure. The materials and procedures in the declaration were either disclosed in the specification or were publicly available as of the filing date of the application. The fact that the actual gene therapy experiments were done after the filing date of the application is irrelevant. Moreover, a detailed description of how to carry out such experiments is not required to be in the specification, provided the procedures were available and could be carried out without undue experimentation. The declaration merely confirms what was already disclosed in the application, namely that bone density may be increased by administering a nucleic acid encoding OPG.

The Examiner also cited *Genentech v. Novo Nordisk* 42 USPQ2d 1005 (Fed. Cir. 1997) to support the position that evidence of enablement must be in the specification and not in the knowledge of one skilled in the art. The present situation is different because, unlike *Genentech*, the art clearly points to certain vectors and methods of administration that are suitable for gene therapy. Certain statements in the references cited by the Examiner suggesting that technical hurdles remain in the clinical practice of gene therapy does not change the fact that starting materials and conditions for administering nucleic acids to animals were clearly identified and known to one skilled in the art.

For the reasons set forth above, Applicants maintain that the specification fully enables the claimed invention and respectfully request that the rejection be withdrawn.

Rejection under obviousness-type double patenting

The Examiner has rejected Claims 61, 65-67, 69 and 73-76 under obviousness-type double patenting over Claims 1, 2, 11 and 12 of the '740 patent. In making this rejection, the Examiner alleges that the subject matter of the present claims is an obvious variant over the claimed subject matter in the '740 patent (paper no. 17):

> Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to a method comprising administering to a mammal a nucleic acid encoding and expressing OPG for treating bone loss (or increase bone density).

The Examiner's position on double patenting is inconsistent with the enablement rejection. In the first instance, the present specification is a continuation-in-part application of the '740 patent and therefore discloses everything (and more) that was contained in the disclosure of the '740 patent . If, as the Examiner alleges, the present claims are not patentably distinct from Claims 1, 2, 11 and 12 of the '740 patent, then the claimed subject matter cannot, on the one hand, be enabled in the '740 patent (as patents are presumed to be enabled) and yet not be enabled in the present application. The Examiner has not pointed out how the presently claimed subject matter differs from that of the '740 patent such that a different determination of enablement would result. In fact, the claims are in enabled in both instances for the reasons set forth in this response.

Nonetheless, if the Examiner withdraws all other outstanding rejections, Applicants will consider the filing of a terminal disclaimer to obviate the obviousness-type double patenting rejection.

CONCLUSION

Claims 61, 63-67, 69 and 71-76 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

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